

### 2.2.5.2 *Authorized versus licensed*

In Europe, biological drugs are authorized, not licensed. This difference goes back to the laws in the United States that considered biologics to be hazardous to produce, and a license was required to manufacture them. EMA requires a marketing authorization application (MAA), whereas the FDA requires a biological license application.

### 2.2.5.3 *Medicines versus drugs*

The EMA prefers to call the treatment modalities as medicines, and the FDA, drugs or biologics.

### 2.2.5.4 *Similarity versus comparability*

Comparability simply means comparing two products, but this vocabulary can be confusing because of the official exercise of Comparability Protocol (ICH [International Conference on Harmonisation] Q5E: Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process), which is a well-defined task for changing the manufacturing process of a licensed product. The change is made by filing specific documents with the regulatory authorities. The similarity is a demonstration of the extent of the sameness of the products being developed. Unfortunately, biosimilar guidelines in the EMA often refer to similarity as comparability, and this should be avoided. *Comparability* is frequently used in lieu of similarity testing. EMA explains: “If the biosimilar *comparability* exercise indicates that there are relevant differences between the intended biosimilar and the reference medicinal product making it unlikely that biosimilarity will eventually be established, a stand-alone development to support a full Marketing Authorisation Application (MAA) should be considered instead.” Some have begun to differentiate between the two comparability exercises as internal (to comply with Q5E when the existing product is compared to a proposed changed product) or external, where a reference product is compared to a biosimilar candidate. The FDA does not condone this vocabulary, and the testing of biosimilar products is a similarity exercise. Also, it should be noted that biosimilarity is an assessment, not an exercise.

### 2.2.5.5 *Effectiveness versus efficacy*

Efficacy is a demonstration of clinical response in a controlled trial; effectiveness is a comparison of the clinical responses of two products. Unfortunately, both the EMA and the World Health Organization (WHO) got it wrong and used the word *efficacy* in describing the evaluation of biosimilars. The FDA did not. In the U.S. guidelines, *efficacy* is not the term used to compare the relative effectiveness, which is distinctly different from efficacy. See the comments of the FDA discussed earlier regarding enoxaparin approval.